

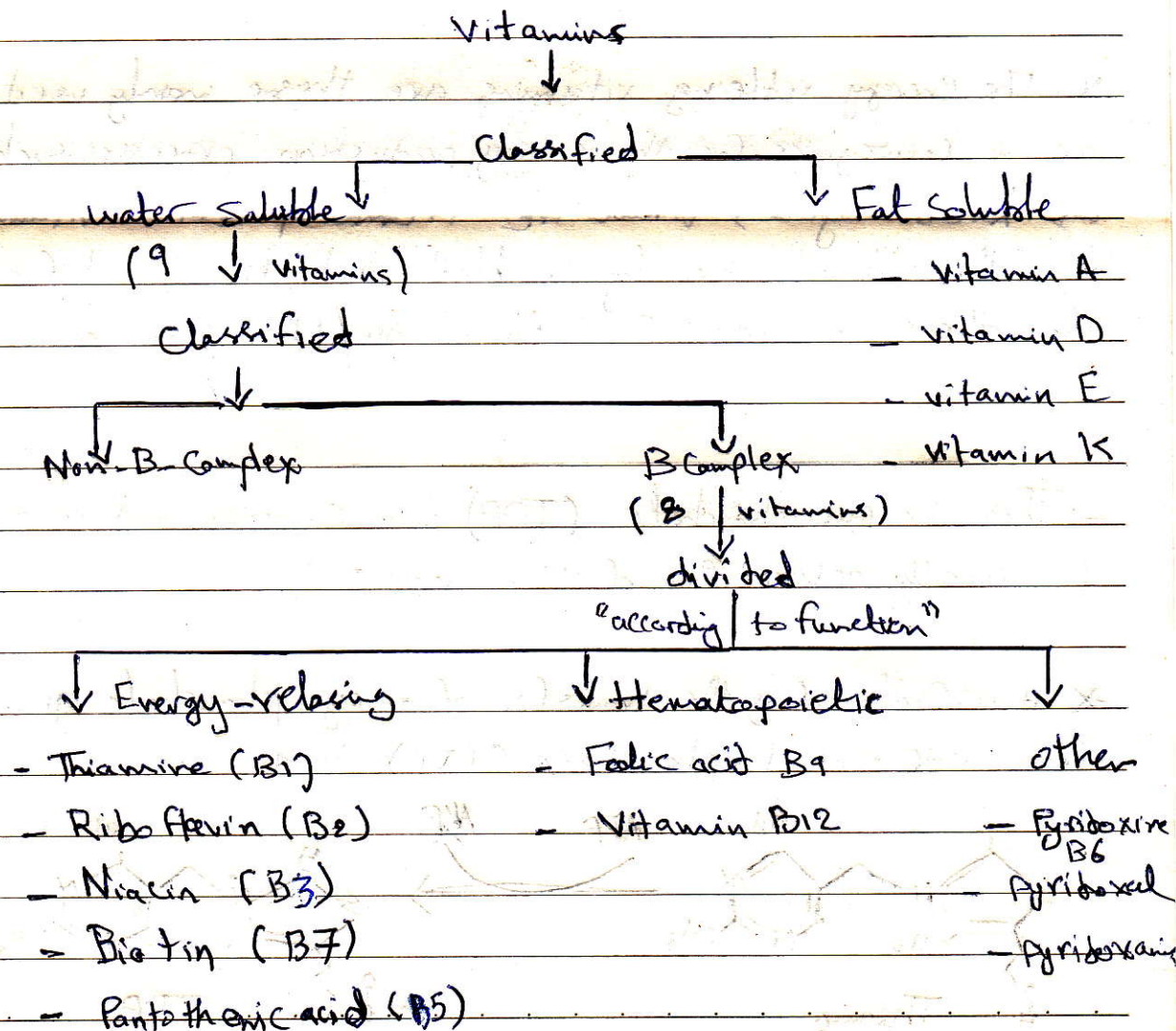
Coenzymes and Vitamins

Vitamin B₁ (thiamine)

Components: Composed of two (thiazole ring + substituted Pyrimidine ring)

Coenzymes and vitamins (review)

* Vitamins: are organic compounds required by the body in trace amounts to perform specific cellular functions.



* Vitamins: our body is unable to synthesize them or synthesize them in insufficient amounts

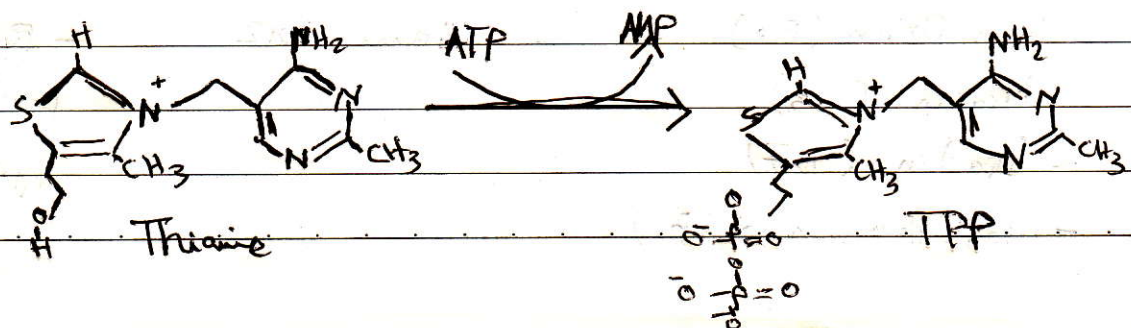
* all water soluble vitamins are Coenzymes either directly or indirectly, but for the fat soluble vitamins vitamin K is the only one that functions as a Coenzyme.

* Fat Soluble vitamins are toxic if taken in large amounts and vitamins A, D are the most toxic where vitamin E is the least toxic.

* The energy releasing vitamins are those mainly used as, a Coenzymes for the energy production processes such as Krebs cycle, while the Hematopoietic vitamins are those used mainly in blood production, and for the others are used for both energy/blood production processes.

- Thiamine pyrophosphate (TPP) is a Coenzyme, and is the biologically active form of Thiamine (B₁)

* It is formed by the transfer of a pyrophosphate group from adenosine triphosphate (ATP) to thiamine



* It consists of two rings Thiazole ring, and substituted pyrimidine ring and two phosphate groups, the two rings are linked by a methyl bridge.

- Clinical indications for thiamine

The activity of the oxidative decarboxylation of pyruvate and α -Ketoglutarate is decreased (the two dehydrogenase-catalyzed reaction is decreased) resulting in a decrease in ATP production (when thiamine is absent)

- thiamine-deficiency diseases;

1- Beriberi :- Severe Thiamine-deficiency Syndrome, adult deficiency is characterized by dry skin, irritability, disordered thinking, and progressive paralysis and in Infants the signs are :- The tachycardia, Vomiting, Convulsions and if not treated it causes death.

2- Wernicke - Korsakoff Syndrome: is a thiamine deficiency associated with chronic alcoholism, is due to dietary insufficiency or impaired intestinal absorption of the vitamin. It is characterized by :- apathy, loss of memory, ataxia and a rhythmic to-and-fro motion of the eye balls (nystagmus) it is treatable with supplementation of thiamine.

* Thiamine deficiency is diagnosed by an increase of transketolase activity observed on addition of TPP.

- **Flavin - Coenzymes (FMN and FAD)**: Flavin mononucleotide (FMN) and Flavin adenine dinucleotide (FAD) are the two biologically active forms (Coenzymes of riboflavin (B₂))

- **FMN** = vit. B₂ + Phosphate group

- **FAD** = FMN + AMP

* FMN and FAD are each capable of reversibly accepting two hydrogen atoms, forming **FMNH₂** or **FADH₂**

* Both are involved in oxidation-reduction reactions

* **Riboflavin** is considered as a nucleotide consisting of Nitrogen base (isoxaloxazine ring), a **Sugar** (Ribitol, sugar alcohol) and a phosphate group

* **Riboflavin deficiency** is not associated with a major human disease, although it frequently accompanies other vitamin deficiencies

* **B₂ deficiency** is characterized by dermatitis, cheilosis, and glossitis.

- Pyridine nucleotides (NAD^+ and NADP^+):

Nicotinamide adenine dinucleotide (NAD^+) is a biologically active coenzyme composed of two parts

- 1- Nicotinamide nucleotide
- 2- Adenine nucleotide (AMP)

* (NADP^+) Nicotinamide adenine dinucleotide phosphate is another biologically active coenzyme

* Both NAD^+ and NADP^+ are capable of accepting a H^- Hydride ion forming $\text{NADH} + \text{H}^+$ or $\text{NADPH} + \text{H}^+$ respectively.

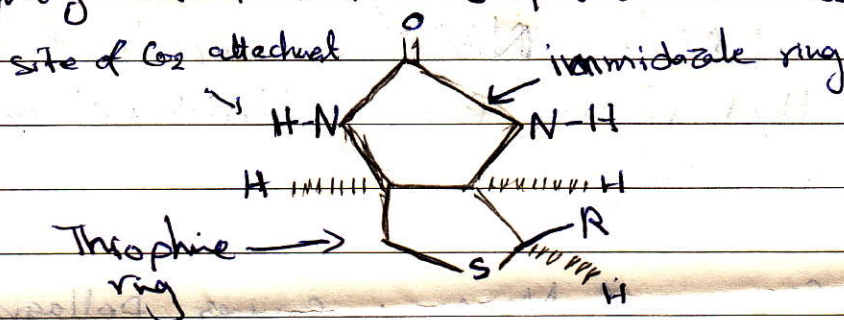
* Deficiency of Niacin: Causes pellagra, a disease involving the skin, gastrointestinal tract, and CNS. The symptoms of pellagra progress through the three Ds: dermatitis, diarrhea, dementia - and if not treated death.

* As a treatment of hyperlipidemia:-

Niacin at high doses strongly inhibits lipolysis in adipose tissue, which results in lowering VLDL and LDL, therefore Niacin is particularly useful in the treatment of type IIb hyperlipoproteinemia.

* **Biotin**: (Vitamin H), is covalently bound to the ϵ -amino group of lysine residue of biotin dependent enzyme. The coenzyme form is called as biocytin. It's a coenzyme in carboxylation reactions, in which it serves as a carrier of activated carbon dioxide (CO_2)

* Raw egg white contains a glycoprotein called **Avidin** that tightly binds to biotin and prevents its absorption



Biotin B6

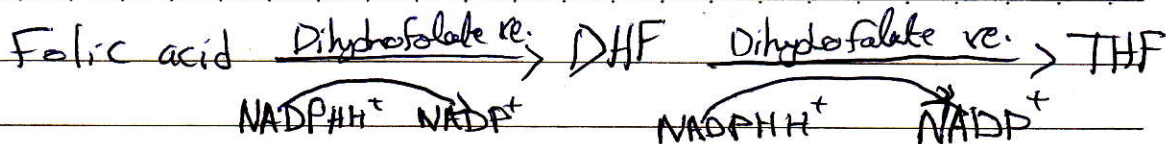
* B6 is usually found attached to **valeric acid** ($(\text{CH}_2)_4\text{COOH}$)

* **Coenzyme A (CoA \approx 8H)**:-

Coenzyme A is the biologically active form of the vitamin pantothenic acid. It functions in the transfer of acyl groups. Coenzyme A contains a thiol ($-\text{SH}$) group that carries acyl compounds as activated thiol esters.

* **Folic Acid B9 (Folate)**:-

Folic acid (or folate) is the vitamin. The biologically active (coenzyme) form of folic acid is tetrahydrofolic acid (THF), which is produced by the two-step reduction of folate by dihydrofolate reductase.



* NADPHH^+ is needed as H donor for the reduction reaction.

* The one carbon unit or fragment is attached to folic acid at Carbon 5

* Cobalamin (B₁₂)

Cobalamin contains a Corrin ring system, The Coenzyme forms of Cobalamin are 5'-deoxyadenosylcobalamin and Methylcobalamin

Corrin rings = tetrapyrrole

* Cobalamin is required in humans for two essential enzymatic reactions: The remethylation of homocysteine to methionine and the isomerization of methylmalonyl Coenzyme A